REMARKS

I. Status of the Claims

Claims 1-118, 120-123, 125, 126, 129-151, 154-169, 171-177, 183-185, 187, 189-191, 197, 198 and 200-202 were pending with the March 24, 2011 Office Action. Of those, claims 2-5, 7-10, 12-42, 46, 53, 55-58, 61-74, 77-96, 98-108, 110-118, 121-123, 129-150, 154-156, 158-160, 171-177, 183, 185, 187, 189, 190, 197, 198 and 200-202 are withdrawn and claims 1, 6, 11, 43-45, 47-52, 54, 59, 60, 75, 76, 97, 109, 120, 125, 126, 151, 157, 161-169, 184 and 191 were examined in the March 24, 2011 Office Action. With this Reply, claims 1, 120, 125 and 151 are amended, claims 2-123, 126, 129-150, 154-169, 171-177, 183-185, 187, 189-191, 197, 198 and 200-202 are newly canceled, and claims 206-210 are newly added. Claims 207-210 are withdrawn as being directed to nonelected species. The claim amendments and additions are made without prejudice or disclaimer and provide no new matter. Support for the claim amendments and additions are provided at least at paragraph **[0043]** at p. 2, and paragraphs **[0053]** to **[0125]** at pp. 3-8 of the specification as published as US 2004/0171557. Claims 1, 120, 125, 151, 206 and 207 are presented for reconsideration.

II. Rejection under 35 U.S.C. § 112, Second Paragraph - Indefiniteness

Claim 169 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite. This rejection is moot since the subject claim is canceled.

III. Rejection under 35 U.S.C. § 112, First Paragraph – Written Description

(a) Claims 1, 6, 11, 43-45, 47-52, 54, 59, 60, 75, 76, 97, 109, 120, 125, 126, 151, 157, 161-169, 184 and 191 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Office Action asserts that the recitation of "β" in β-glycosylceramide is new matter. This rejection is moot since the claims as amended do not recite β-glycosylceramide. In this regard, Applicants note

that the Office Action, on p. 3, points to Adar and Ilan, 2008, J. Immunotoxicology 5:209-220, as establishing that no alpha-glycosylceramides have been detected in mammals. As such, since the claims are directed to the use of mammalian intermediary metabolites, no reference that teaches the use of an alpha-glycosylceramide would anticipate the instant claims.

(b) Claims 1, 6, 11, 43-45, 47-52, 54, 59, 60, 75, 76, 97, 109, 120, 125, 126, 151, 157, 161-169, 184 and 191 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Office Action asserts that the specification does not provide sufficient support for "β-glycosylceramide" for its full scope. In response, Applicants note that, while the Office Action cites Sweeley, 1989, Pure & Appl. Chem. 61:1307-12 for the proposition that there are enormous numbers of glycosphingolipids having a huge heterogeneity of structure, the claims as amended are directed to the use of mammalian glycosylceramides, a much smaller subset of compounds that are structurally much more homogeneous than glycosphingolipids, since they comprise only sugar and ceramide moieties. Additionally, different mammalian glycosylceramides are known to have similar activities. To support that statement, Applicants point to Motoki et al., 1995, Biol. Pharm. Bull. 18:1487-91, provided herewith. In particular, Applicants point to FIG. 2, on p. 1490 of that reference, where lymphocytic proliferation stimulatory effects of various glycosylceramides are compared. Of relevance for this discussion, Applicants point to AGL-564 and AGL-562, which are β-galactosylceramide (β-GalCer) and β-glucosylceramide (β-GluCer), respectively – see p. 1469 under RESULTS AND DISCUSSION for confirmation of the identification of those monosaccharide ceramides. As shown in FIG. 2, β-GalCer and β-GluCer (shown in the bars having diagonal hatch marks and horizontal hatch marks, respectively) showed very similar activity, while α compounds (not of mammalian origin), having sold filled bars, showed greater activity than the two β- compounds. Thus, Motoki et al. would lead the skilled artisan to understand that all mammalian glycosylceramides would be expected to have similar activities.

To confirm the expectation at the time of filing that any glycosylceramide would be expected to be effective in the claimed method, Applicants provide the post-filing reference Zigmond et al., 2008, Am. J. Physiol. Endocrinol. Metab., showing that both β-glucosylceramide (i.e., glucocerebroside) and β-lactosylceramide (a disaccharide ceramide) are effective in improving glucose tolerance and hepatic steatosis.

In light of the above discussion, it is clear that the claims are described sufficiently such that the skilled artisan would understand that the Applicants had possession of the claimed invention for its full scope. Withdrawal of the written description rejection under 35 U.S.C. 112, first paragraph, is therefore respectfully requested.

IV. Rejection under 35 U.S.C. § 112, First Paragraph – Enablement

Claims 1, 6, 11, 43-45, 47-52, 54, 59, 60, 75, 76, 97, 109, 120, 125, 126, 151, 157, 161-169, 184 and 191 are rejected under 35 U.S.C. 112, first paragraph, enablement requirement. The Office Action asserts that the specification "...does not reasonably provide enablement for the treatment of any and all diseases derived from an inflammatory immune response in a mammalian subject comprising administering any and all beta-glycosylceramide." Office Action at p. 9. Applicants request reconsideration and withdrawal of this rejection in light of the claim amendments and the following discussion.

Regarding the objection to the breadth of the metabolites recited in the claims, Applicants note that the claims as amended are directed only to treatments with monosaccharide ceramides, which, as further discussed under **III.** above, are known as a structurally similar class of compounds with similar activities, that includes the glucocerebroside (β-glucosylceramide) utilized in the Examples. As such, the claims as amended involve treatment with a limited group of structurally similar compounds known to have generally similar biological activities. The skilled artisan would therefore understand that the claimed methods would be effective with most if not all mammalian glycosylceramides. Additionally, any particular glycosylceramide can be tested for

effectiveness for the instant methods (i.e., as modulating an inflammatory immune response) without undue experimentation, for example using the methods described in the examples.

Regarding the objection to the breadth of the diseases in the claims, Applicants first note that the claims as amended are directed to treatment of colitis, immune-mediated hepatitis, nonalcoholic steatohepatitis, diabetes or melanoma. The specification provides data, at least at paragraphs **[0053]** – **[0125]** at pp. 3-8 of the publication US 2004/0171557 demonstrating the effective treatment of each of the recited diseases in mice. Thus, working examples for each recited disease is provided. Thus, the specification provides sufficient guidance for practicing the claimed methods to allow the skilled artisan to practice the methods as claimed without undue experimentation.

In light of the claim amendments and the above discussion, Applicants respectfully request withdrawal of the enablement rejection under 35 U.S.C. 112, first paragraph.

VI. Double Patenting Rejections

Claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 109, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of obviousness-type double patenting (ODP) as being unpatentable over claims 1, and 4-6 of copending Application No. 10/375,906 in view of Stephenson and Zambon (Occup. Med, 2002). Also, claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of obviousness-type double patenting (ODP) as being unpatentable over claims 50-52, 55-57, 59 and 60 of copending Application No. 10/733,488 in view of Stephenson and Zambon (Occup. Med, 2002) and Hansen-Flaschen (Ann Intern Med, 2003). Additionally, claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 109, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of obviousness-type double patenting (ODP) as being unpatentable over claims 12, 16, 17, 20, 22-24 and 64 of copending Application No. 10/733,489 in view of Stephenson and Zambon (Occup. Med, 2002)

and Hansen-Flaschen (Ann Intern Med, 2003). Further, claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of obviousness-type double patenting (ODP) as being unpatentable over claims 77-100 of copending Application No. 11/287,502. Still further, claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of obviousness-type double patenting (ODP) as being unpatentable over claims 1, 2 and 5 of copending Application No. 12/746,430. Since these rejections are dependent on the scope of both the instant claims and the claims in the cited applications, Applicants will provide a terminal disclaimer where necessary when a proper ODP rejection is the only rejection remaining in this application.

VII. Conclusion

In view of the foregoing remarks, Applicants respectfully request withdrawal of the rejections of record and examination of withdrawn claims 208-211, since those withdrawn claims have all the limitations of claim 1.

Applicants authorize the United States Patent and Trademark Office to charge all fees required to maintain pendency of this application, including the extension of time and Request for Continued Examination fees, to Deposit Account No. 05-1135.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney requests that he be contacted at the number provided below.

Respectfully submitted,

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